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MARSHALL, GERSTEIN & BORUN LLP
233 S. WACKER DRIVE, SUITE 6300
SEARS TOWER
CHICAGO, IL 60606

EXAMINER	
MITRA, RITA	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/629,516	HORWITZ ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☒ Claim(s) *1-19* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Applicants' preliminary amendment, filed on July 29, 2003 is acknowledged. Amendment to the specification is noted. Claims 1-19 are currently pending and are under examination.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-3 and 13-16, drawn to polypeptides, which are BPI deletion analogs, and, classified in class 530, subclass 350, 300.

I I. Claims 4-12, drawn to polynucleotides encoding BPI deletion analogs, an expression vector, host cells and a process for producing the BPI polypeptides recombinantly, classified in class 435, subclass 69.1, 320.1, 253.3, 325.

III. Claims 17-19, drawn to methods of administering BPI protein products to a subject, classified in class 514, subclass 12.

The inventions are distinct, each from the other because of the following reasons:

The polypeptides of group I are related to the DNAs of group II by virtue of the fact that the DNA codes for the protein. The DNA molecule has utility for the recombinant production of the protein in a host cell. Although the DNA and the protein are related, since the DNA encodes the specifically claimed protein, they are distinct inventions because the protein product can be made by other and materially distinct processes such as by synthetic peptide synthesis or purification from the natural source. Further, DNA can be used for processes other than the production of protein, such as nucleic acid hybridization assays. Therefore, the inventions are

distinct. Inventions in Group I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP ' 806.04, MPEP ' 808.01). In the instant case the polypeptide of Group I and the polynucleotide of Group II differ with respect to their structure, and their physical, chemical and biological properties and function. The peptides of Group I can be used to make antibodies, while polynucleotides of Group II can be used for hybridization assay. Therefore, the inventions are patentably distinct.

Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP 806.05(h)). In the instant case the polypeptide of invention I can be used on other, materially distinct processes, such as in methods for the production of antibody, for example. Therefore, the inventions are distinct.

Inventions II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP 806.04, MPEP 808.01). In the instant case the invention III is directed to a process whose end result is materially distinct from the recombinant process of invention II. The results of the processes are directed to different ends. Therefore, the inventions are distinct.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection

are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

During a telephone conversation with Attorney Ann Doland on October 20, 2005 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-3, 13-16. Affirmation of this election must be made by applicant in replying to this Office action.

Upon further consideration claims 4-12, 17-19 found to be examined together with claims 1-3 and 13-16. Therefore, claims 4-12 and 17-19 are joined with claims 1-3, 13-16 and the Restriction Requirement (supra) is withdrawn. Thus claims 1-19 are under examination in the instant application.

Objection to the Specification

Abstract is objected to because of the following informalities:

The abstract should include the steps in the methods of the invention.

The specification is objected to because the specification describes sequences that are set forth in the "Sequence Listing" and embedded in the text of the specification at pages 2, 31, Figure 3, however no reference is made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" See 37 C.F.R. § 1.181(d). This objection may be overcome by providing sequence identifier to the embedded sequences.

The continuing data starting at the first page, first line should be updated.

Claim Rejections - 35 USC § 101-Nonstatutory

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 4 and 5 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. These claims recite "A polynucleotide" which reads on the natural, non-patentable, state of the polynucleotide. The rejection would be obviated by the insertion of language indicating that the polynucleotide was isolated and/or purified, thus being removed from the natural environment.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-19 are objected to because the claims describe a sequence that is set forth in the "Sequence Listing" and embedded in the text of the specification, however no reference is made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" See 37 C.F.R. § 1.181(d). This objection may be overcome by providing sequence identifier to the claims.

Claim 6 is indefinite for reciting "...the twenty seven amino acid leader sequence of BPI." It is not clear which BPI is this.

Claims 17-19 are indefinite because of the use of the term "improved method". This term renders the claims indefinite. It is not clear what an "improved method " is or what is the improvement, (use Jepsen claim format for improvement). What is that method from where the claimed method has been improved? What is the limitation of this "improved method" in relation to the method from which it has been improved? Is the improvement in the method of administration or in the product composition, which is being administered?

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to

> which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 and 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horwitz *et al.* (Protein Expression and Purification, vol. 8, pp 28-40, 1996) in view of Capodici *et al.* (J. of Immunology, vol. 156, pp 4789-4796, 1996) and further in view of Little (US 5,652,332, 1997).

Horwitz *et al.* teach (i) that the recombinant N-terminal portion of BPI (residues 1-199) retains bactericidal activity (page 28, Introduction, right column, lines 8-14), (ii) a DNA encoding the first 193 amino acids (with or without the desired cysteine mutations)," (page 29, section entitled 'Construction of Expression plasmids containing rBPI193), (iii) a recombinant BPI consisting of residues 1-193 with a C132A mutation (Figure 1, page 30) and (iv) that a C132A modification yields a stable, biologically active, N-terminal BPI fragment (designated $rBPI_{21}$) that is free of dimeric species (page 28, Abstract, right column, lines 6-8). The C132A mutation resulted in a polypeptide that contained no free thiol groups (page 37, right column, lines 6-13) thus preventing cross-linking and dimerization, which teaches that substitution of cysteine with any amino acid not containing sulfur at this position

would produce similar biological results as the C132A mutation. Horwitz et al. do not teach truncation to amino acids 10-193.

Capodici et al. teach human BPI peptide fragments that are amino acids 1-193 and 13-193 (page 4792, right column, line 8) where the similarity of LPS-binding of BPI_{1-193} and BPI_{13-193} indicates that the N-terminal 12 amino acids of BPI are not needed for LPS recognition (page 4793, left column, lines 1-3) and deletion of the N-terminal 12 residues did not diminish BPI function (Abstract). It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the recombinant BPI_{1-193} C132A mutation protein of Horwitz et al., from which **any** (emphasis added) of the first 12 amino acids may be deleted without affecting function, including amino acids 1-9, resulting in a BPI_{10-193} C132A mutation protein (truncation taught by Capodici et al.) to produce the invention of claims 1-3 and 13. The motivation to combine the teachings of Horwitz and Capodici would come from the desire to produce a recombinant human BPI protein that retains bactericidal activity and maintains structural/functional stability. This combination would result in more efficient production of a human bactericidal BPI protein.

Horwitz and Capodici do not teach a composition comprising a BPI_{10-193} C132A mutation protein and a pharmaceutically-acceptable carrier (claims 14-16). Little (US '332) teaches the use of pharmaceutically-acceptable carriers with human BPI proteins (Column 5, lines 33-43). It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Little with the combined teachings of Horwitz and Capodici references to arrive at the invention of claims 14-16. The motivation to combine the teaching of Little with the combined teachings of Horwitz and Capodici would come from the desire to administer the recombinant BPI_{10-193} C132A mutation protein in a formulation that would take advantage of the bactericidal properties of said protein for administration in an infected animal.

Claims 1-3 and 13-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horwitz *et al.* (Protein Expression and Purification, vol. 8, pp 28-

40, 1996) in view of Capodici *et al.* (J. of Immunology, vol. 156, pp 4789-4796, 1996) and further in view of Little (US 5,652,332, 1997) as applied to claims 1-3 and 13-16 above, and further in view of McGregor *et al.* (US 5,488,034).

McGregor *et al.* teach administration of bactericidal permeability increasing (BPI) protein (see the examples) where the BPI had a mutation at position 132 (see column 5 of the patent), where cysteine is replaced with an alanine. While the McGregor *et al.* patent did not specifically disclose deletion of the first 10 or so amino acids, McGregor *et al.* nevertheless used active fragments of BPI such as $rBPI_{12}$ or any amino-terminal fragment comprising from about the first 193-199 amino terminal amino acid residues of BPI are believed to be susceptible to loss of stability in aqueous solution (column 2). Where McGregor *et al.* also teach using active fragments and that the N-terminus is important to biological function. Horwitz *et al.*, Capodici *et al.* and Little et al. have been applied here as indicated above. In addition where McGregor discusses BPI, where the BPI had a mutation at position 132, BPI active fragments and that the N-terminal is important to biological function and is directed to using minimum structural requirements and that deletion of some 12 residues from the N-terminus is without effect on LPS binding, it would have been obvious to one of ordinary skill in the art to have modified the peptides disclosed in the McGregor *et al.* reference by N-terminal truncation for the advantages of using a minimal structure for the active agent. Thus, the process of claims 17-19 of administering a BPI to a subject would have, from the combined cited references have been obvious since the combined references teach administering BPI modified in a manner identical if not similar to that recited in the claims and would have been in an appropriate carrier (see, e.g., McGregor *et al.* at column 3 and example 4, *et seq.*). Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

Rejections - Nonstatutory Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 13-16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, of **U.S. Patent 6,013,631.** Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-3 and 13-16 are directed to the broadest scope of the BPI protein deletion analogs and a composition comprising said analogs.

Claims 1-3 disclose a bactericidal/permeability-increasing (BPI) protein deletion analogs consisting of amino acid residues 10 through 193 of mature human BPI (SEQ ID NO: 2) wherein a cysteine residue at position 132 is replaced by a different amino acid **(claim 1)**, wherein said amino acid is a non-polar amino acid selected from the group consisting of alanine and serine **(claim 2)**, wherein the cysteine residue at position 132 is replaced by alanine **(claim 3).** This is an obvious variation of claims **1-3** in the **patent '631**, which discloses a bactericidal/permeability-increasing (BPI) protein deletion analogs consisting of amino acid residues 10 through 193 of mature human BPI (SEQ ID NO: 2) wherein a cysteine residue at position 132 is replaced by a different amino acid and wherein the amino acid at position 185 is selected from the group consisting of lysine and glutamic acid **(claim 1 '631)**, wherein said amino acid is a non-polar amino acid selected from the group consisting of alanine and serine **(claim 2 '631)**, wherein the cysteine residue at position 132 is replaced by alanine **(claim 3**

'631). It should be noted here that though the claim 1 of instant application does not require the amino acid lysine or glutamic acid at position 185, the SEQ ID NO: 2 sequence has a lysine in position 185 (see SEQ ID NO: 2 in the sequence listing), thus it is expected that the sequence 2 in claim 1 would have a lysine in position 185. Thus this is obvious over prior art US '631.

Claims 13-16 disclose a polypeptide product of a method of producing BPI protein deletion analogs, comprising growing a host cell transformed with a DNA encoding the BPI deletion analog polypeptide of claim 1 of instant claims (**claim 13**), wherein a composition comprising said BPI deletion analog of said polypeptide product and a pharmaceutically-acceptable diluent, adjuvant, or carrier (**claim 16**). **Claim 14** is drawn to a composition comprising the BPI deletion analog of claim 1 and a pharmaceutically-acceptable diluent, adjuvant, or carrier. **Claim 15** is drawn to a composition comprising the BPI deletion analog of claim 3 and a pharmaceutically-acceptable diluent, adjuvant, or carrier. This is an obvious variation of claims **4-7** in the **patent '631**, which discloses a polypeptide product of a method of producing BPI protein deletion analogs, comprising growing a host cell transformed with a DNA encoding the BPI deletion analog polypeptide of claim 1 or 3 of patent '631 (**claim 4 '631**), wherein a composition comprising said BPI deletion analog of said polypeptide product and a pharmaceutically-acceptable diluent, adjuvant, or carrier (**claim 7 '631**). Claim 14 of instant application is an obvious variation of **claim 5 '631** that discloses a composition comprising the BPI deletion analog of claim 1 '631 and a pharmaceutically-acceptable diluent, adjuvant, or carrier. Claim 15 of instant application is an obvious variation of **claim 6 '631** that discloses a composition comprising the BPI deletion analog of claim 3 '631 and a pharmaceutically-acceptable diluent, adjuvant, or carrier.

Claims 4-12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of **U.S. Patent 6,087,126.** Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 4-12 are directed to the broadest scope of the BPI protein deletion analogs that are encoded by an isolated polynucleotide.

Claims 4-12 disclose a polynucleotide encoding the BPI protein deletion analog consisting of amino acid residues 10 through 193 of mature human BPI (SEQ ID NO: 2) wherein

a cysteine residue at position 132 is replaced by a different amino acid (**claim 4**). **Claim 5** discloses a polynucleotide encoding the BPI deletion analog, wherein the cysteine residue at position 132 is replaced by alanine. The polynucleotide of claim 4, which is a DNA (**claim 7**) further comprising the twenty-seven amino acid leader sequence of BPI (**claim 6**). **Claim 8** discloses an expression vector comprising the DNA of claim 7, wherein a host cell is transformed with said DNA in a manner allowing expression in said host cell of said polypeptide deletion analog (**claim 9**), wherein said host cell is a eukaryotic host cell (**claim 10**), wherein said eukaryotic host cell is a CHO cell (**claim 11**). **Claim 12** discloses a method for producing a BPI deletion analog polypeptide comprising growing a host cell of claim 9 and isolating said polypeptide from said host cell culture.

This is an obvious variation of claims **1-9** in the **patent '126**, which disclose a polynucleotide encoding the BPI protein deletion analog consisting of amino acid residues 10 through 193 of mature human BPI (SEQ ID NO: 2), wherein a cysteine residue at position 132 is replaced by a different amino acid and wherein the amino acid at position 185 is selected from the group consisting of lysine and glutamic acid (**claim 1 '126**), wherein said amino acid is a non-polar amino acid selected from the group consisting of alanine and serine (**claim 10 '126**), wherein said cysteine residue at position 132 is replaced by alanine (**claim 2 '126**). It should be noted here that though the claim 1 of instant application does not require the amino acid lysine or glutamic acid at position 185, the SEQ ID NO: 2 sequence has a lysine in position 185 (see SEQ ID NO: 2 in the sequence listing), thus it is expected that the sequence of SEQ ID NO: 2 in claim 1 would have a lysine in position 185. Thus this is obvious over prior art US '126.

The polynucleotide of claim 6, which is a DNA of claim 4 is an obvious variation of **claim 3 '126,** wherein said polynucleotide further comprising the twenty-seven amino acid leader sequence of BPI (SEQ ID NO: 2). Claims 8-11 are obvious variation of **claim 5 '126,** which discloses an expression vector comprising the DNA of **claim 4 '126,** wherein a host cell is transformed with said DNA in a manner allowing expression in said host cell of said polypeptide deletion analog (**claim 6 '126**), wherein said host cell is a eukaryotic host cell (**claim 7 '126**), wherein said eukaryotic host cell is a CHO cell (**claim 8 '126**). Claim 12 of instant application is obvious in view of **claim 9 '126** that discloses a method for producing a BPI deletion analog

polypeptide comprising growing a host cell of **claim 6 '126** and isolating said polypeptide from said host cell culture (**claim 9 '126**).

Claims 17-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-39, of **U.S. Patent 6,599,880.** Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 17-19 are directed to the broadest scope of the method of administering a BPI protein product to a subject comprising a composition comprising the BPI deletion analog and a pharmaceutically-acceptable diluent, adjuvant or carrier.

Claims 17-19 disclose an improved method of administering a BPI protein product to a subject comprising a composition comprising the BPI deletion analog and a pharmaceutically-acceptable diluent, adjuvant or carrier consisting of amino acid residues 10 through 193 of mature human BPI (SEQ ID NO: 2) wherein a cysteine residue at position 132 is replaced by a different amino acid (**claim 17**), wherein said cysteine residue at position 132 is replaced by alanine (**claim 18),** wherein said polypeptide analog is produced by a method comprising growing a host cell of claim 9 and isolating said polypeptide from said host cell culture (**claim 19**).

This is an obvious variation of claims **1-3** in the **patent '880**, which discloses a method for treating gram-negative bacterial infections in a subject comprising administering a therapeutically effective amount of BPI protein deletion analog consisting of amino acid residues 10 through 193 of mature human BPI (SEQ ID NO: 2) wherein a cysteine residue at position 132 is replaced by a different amino acid and wherein said method results in attenuation of said gram-negative bacterial infection (**claim 1 '880**), wherein the cysteine residue at position 132 is replaced by alanine (**claim 2 '880**), wherein said BPI deletion analog is isolated from the culture of a host cell transformed with DNA encoding said BPI deletion analog (**claim 3'880**).

This is an obvious variation of claims **4-6** in the **patent '880**, which discloses a method for treating gram-positive bacterial infections in a subject comprising administering a therapeutically effective amount of BPI protein deletion analog consisting of amino acid residues 10 through 193 of mature human BPI (SEQ ID NO: 2) wherein a cysteine residue at position 132

is replaced by a different amino acid and wherein said method results in attenuation of said gram-positive bacterial infection (**claim 4 '880**), wherein the cysteine residue at position 132 is replaced by alanine (**claim 5 '880**), wherein said BPI deletion analog is isolated from the culture of a host cell transformed with DNA encoding said BPI deletion analog (**claim 6 '880**).

This is an obvious variation of claims **7-9** in the **patent '880**, which discloses a method for treating mycoplasmal infections in a subject comprising administering a therapeutically effective amount of BPI protein deletion analog consisting of amino acid residues 10 through 193 of mature human BPI (SEQ ID NO: 2) wherein a cysteine residue at position 132 is replaced by a different amino acid and wherein said method results in attenuation of said mycoplasmal infection (**claim 7 '880**), wherein the cysteine residue at position 132 is replaced by alanine (**claim 8 '880**), wherein said BPI deletion analog is isolated from the culture of a host cell transformed with DNA encoding said BPI deletion analog (**claim 9 '880**).

This is an obvious variation of claims **10-12** in the **patent '880**, which discloses a method for treating fungal infections in a subject comprising administering a therapeutically effective amount of BPI protein deletion analog consisting of amino acid residues 10 through 193 of mature human BPI (SEQ ID NO: 2) wherein a cysteine residue at position 132 is replaced by a different amino acid and wherein said method results in attenuation of said fungal infection (**claim 10 '880**), wherein the cysteine residue at position 132 is replaced by alanine (**claim 11 '880**), wherein said BPI deletion analog is isolated from the culture of a host cell transformed with DNA encoding said BPI deletion analog (**claim 12 '880**).

This is an obvious variation of claims **13-15** in the **patent '880**, which discloses a method for treating protozoan infections in a subject comprising administering a therapeutically effective amount of BPI protein deletion analog consisting of amino acid residues 10 through 193 of mature human BPI (SEQ ID NO: 2) wherein a cysteine residue at position 132 is replaced by a different amino acid and wherein said method results in attenuation of said protozoan infection (**claim 13 '880**), wherein the cysteine residue at position 132 is replaced by alanine (**claim 14**

'880), wherein said BPI deletion analog is isolated from the culture of a host cell transformed with DNA encoding said BPI deletion analog (**claim 15 '880**).

This is an obvious variation of claims **16-18** in the **patent '880**, which discloses a method for treating chamydial infections in a subject comprising administering a therapeutically effective amount of BPI protein deletion analog consisting of amino acid residues 10 through 193 of mature human BPI (SEQ ID NO: 2) wherein a cysteine residue at position 132 is replaced by a different amino acid and wherein said method results in attenuation of said chamydial infection (**claim 16 '880**), wherein the cysteine residue at position 132 is replaced by alanine (**claim 17 '880**), wherein said BPI deletion analog is isolated from the culture of a host cell transformed with DNA encoding said BPI deletion analog (**claim 18 '880**).

This is an obvious variation of claims **19-21** in the **patent '880**, which discloses a method for treating mycrobacterial infections in a subject comprising administering a therapeutically effective amount of BPI protein deletion analog consisting of amino acid residues 10 through 193 of mature human BPI (SEQ ID NO: 2) wherein a cysteine residue at position 132 is replaced by a different amino acid and wherein said method results in attenuation of said mycobacrterial infection (**claim 19 '880**), wherein the cysteine residue at position 132 is replaced by alanine (**claim 20 '880**), wherein said BPI deletion analog is isolated from the culture of a host cell transformed with DNA encoding said BPI deletion analog (**claim 21 '880**).

This is an obvious variation of claims **22-24** in the **patent '880**, which discloses a method for treating meningococcemia in a subject comprising administering a therapeutically effective amount of BPI protein deletion analog consisting of amino acid residues 10 through 193 of mature human BPI (SEQ ID NO: 2) wherein a cysteine residue at position 132 is replaced by a different amino acid and wherein said method results in attenuation of said meningococcemia (**claim 22 '880**), wherein the cysteine residue at position 132 is replaced by alanine (**claim 23 '880**), wherein said BPI deletion analog is isolated from the culture of a host cell transformed with DNA encoding said BPI deletion analog (**claim 24 '880**).

This is an obvious variation of claims **25-27** in the **patent '880**, which discloses a method for treating hemorrhagic trauma in a subject comprising administering a therapeutically effective amount of BPI protein deletion analog consisting of amino acid residues 10 through 193 of mature human BPI (SEQ ID NO: 2) wherein a cysteine residue at position 132 is replaced by a different amino acid and wherein said method results in attenuation of said hemorrhagic (**claim 25 '880**), wherein the cysteine residue at position 132 is replaced by alanine (**claim 26 '880**), wherein said BPI deletion analog is isolated from the culture of a host cell transformed with DNA encoding said BPI deletion analog (**claim 27 '880**).

This is an obvious variation of claims **28-30** in the **patent '880**, which discloses a method for treating ischemia/reperfusion injury in a subject comprising administering a therapeutically effective amount of BPI protein deletion analog consisting of amino acid residues 10 through 193 of mature human BPI (SEQ ID NO: 2) wherein a cysteine residue at position 132 is replaced by a different amino acid and wherein said method results in attenuation of said ischemia/reperfusion injury (**claim 28 '880**), wherein the cysteine residue at position 132 is replaced by alanine (**claim 29 '880**), wherein said BPI deletion analog is isolated from the culture of a host cell transformed with DNA encoding said BPI deletion analog (**claim 30 '880**).

This is an obvious variation of claims **31-33** in the **patent '880**, which discloses a method for treating an angiogenesis-associated disorder in a subject comprising administering a therapeutically effective amount of BPI protein deletion analog consisting of amino acid residues 10 through 193 of mature human BPI (SEQ ID NO: 2) wherein a cysteine residue at position 132 is replaced by a different amino acid and wherein said method results in attenuation of said angiogenesis-associated disorder (**claim 31 '880**), wherein the cysteine residue at position 132 is replaced by alanine (**claim 32 '880**), wherein said BPI deletion analog is isolated from the culture of a host cell transformed with DNA encoding said BPI deletion analog (**claim 33 '880**).

This is an obvious variation of claims **34-36** in the **patent '880**, which discloses a method for treating a thrombic disorder in a subject comprising administering a therapeutically effective amount of BPI protein deletion analog consisting of amino acid residues 10 through 193 of

mature human BPI (SEQ ID NO: 2) wherein a cysteine residue at position 132 is replaced by a different amino acid and wherein said method results in attenuation of said thrombic disorder (**claim 34 '880**), wherein the cysteine residue at position 132 is replaced by alanine (**claim 35 '880**), wherein said BPI deletion analog is isolated from the culture of a host cell transformed with DNA encoding said BPI deletion analog (**claim 36 '880**).

This is an obvious variation of claims **37-39** in the **patent '880**, which discloses a method for treating the effects of endotoxin in the circulation of a subject comprising administering a therapeutically effective amount of BPI protein deletion analog consisting of amino acid residues 10 through 193 of mature human BPI (SEQ ID NO: 2) wherein a cysteine residue at position 132 is replaced by a different amino acid and wherein said method results in attenuation of said effects of endotoxin (**claim 37 '880**), wherein the cysteine residue at position 132 is replaced by alanine (**claim 38 '880**), wherein said BPI deletion analog is isolated from the culture of a host cell transformed with DNA encoding said BPI deletion analog (**claim 39 '880**).

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita Mitra whose telephone number is 571-272-0954. The examiner can normally be reached on M-F, 10:00 am-7:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
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Rita Mitra, Ph.D.
November 7, 2005

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER